

Sex Difference in the Association between Sleep Duration and Thyroid Disease among South Korean Adults

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Objectives: The study aimed to investigate sex differences associated with sleep duration and the prevalence of thyroid disease among South Korean adults. **Methods:** This cross-sectional study included 17,555 adults who participated in the Korea National Health and Nutrition Examination Survey from 2016 to 2018. Sleep duration was categorized into three groups (insufficient, <7 hour; normal, 7-8 hour; prolonged, ≥9 hour). A chi-squared test was performed to assess baseline characteristics. Multiple logistic regression analysis was used to identify the association between general characteristic and the prevalence of thyroid disease. In subgroup analysis, multiple logistic regression analysis was performed to find the association between sleep duration and prevalence of thyroid disease by sex. **Results:** For men, insufficient and prolonged sleep durations were increased risk of thyroid disease compared with normal sleep duration (insufficient sleep: odds ratio, OR = 1.85, 95% confidence interval, CI = 1.19-2.87; prolonged sleep: OR = 1.71, 95% CI = 1.02-2.87). **Conclusions:** This study found that men with insufficient and prolonged sleep were associated with thyroid disease. Further studies are needed to identify the relationship between sleep duration, thyroid disease, and sleep quality by sex.

Key words: Sex difference, Sleep duration, Thyroid disease

INTRODUCTION

Sleep is an important component of health status. Although many people recognize that sleep is essential for life, they do not complete the required sleep duration due to social, leisure, or business-related activities [1]. If the situation persists, it can negatively affect lifestyle and mental status and can lead to the occurrence of several diseases. In particular, insufficient sleep aggravates depression, physical health, immune, cardiovascular, and metabolic syndrome [2]. It affects patients with chronic pain and physical and psychological symptoms [3]. Sleep is related to an increased risk of mortality [4] and affects metabolic syndrome by sex [5]. Increased risk of all-cause mortality such as ischemic heart disease, other heart disease, cerebrovascular accidents, cancer, suicide and homicide were associated with short and long sleep duration [4]. Concerning metabolic syndrome, men are associated with short sleep duration, and

women are affected by long sleep duration [5]. Therefore, it is essential to sleep properly to maintain adequate sleep duration and prevent diseases.

There are many thyroid diseases such as autoimmune disease and Graves' disease, which cause hyperthyroidism and Hashimoto's thyroiditis, which results in hypothyroidism [6]. Based on the reference range of serum thyroid stimulating hormone (TSH) (0.62-6.68 mIU/L), the prevalence of subclinical hypothyroidism and subclinical hyperthyroidism was 0.73% (0.40% men, 1.10% women) and 3.10% (2.26% men, 4.04% women), respectively, in Korea, from 2013-2015 [7]. Previous studies have investigated the association between sleep and thyroid diseases [8]. Sleep can affect hormone secretion, thyroid dysfunction, subclinical hyperthyroidism, and subclinical hypothyroidism [8]. Insufficient sleep indicated a significantly increased risk of subclinical hyperthyroidism not hypothyroidism; however, prolonged sleep were elevated risk of subclinical hyperthyroidism and hypothyroidism [8]. A previous study indicated an

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increase in serum concentrations of fT3 and fT4 among individuals with sleep restriction compared to normal sleepers [9]. Furthermore, acute partial sleep deprivation has been shown to be influenced by endocrine homeostasis, health, and wellbeing status [9].

Although numerous studies have shown the associations between sleep duration and thyroid hormones, little is known about whether sleep durations were associated with thyroid disease. Further, few studies have investigated the association between sleep duration and the prevalence of thyroid disease according to sex. Thus, our study examined sleep duration and thyroid disease according to sex among South Korean adults, using data from the Korea National Health and Nutrition Examination Survey (KNHANES) from 2016 to 2018.

METHODS

Study population and database information

The KNHANES is a national questionnaire designed to analyze the health and nutrition stations among Koreans and is often used as primary data. The questionnaire provides objective and standardized sources while estimating the prevalence of diseases, conditions, and risk behaviors [10]. The study data were extracted from the seventh KNHANES, conducted from 2016-2018. First, 24,269 participants were identified from the KNHANES VII-3. We excluded the data collected from participants who were <19 years ($n=4,880$), cases with missing information concerning the average sleep time per day during the weekday ($n=1,116$) and weekend ($n=1$), as well as cases involving no responses concerning average sleep time per day during the weekday ($n=711$) and the weekend ($n=6$). After excluding the data, 17,555 individuals (7,641 men, 9,914 women) were included in this study.

Definition of thyroid disease

Thyroid disease includes autoimmune disease, Graves' disease, Hashimoto's thyroiditis, hyperthyroidism, and hypothyroidism [6]. In this study, participants were classified as having thyroid diseases and not having thyroid disease. Thyroid disease was defined as participants who responded "yes" to the following questions from the KNHANES: 1) Have you been diagnosed with thyroid disease by a physician? 2) Are you currently suffering from thyroid disease? Following these questions, individuals were defined as having thyroid disease diagnosed by a physician and currently suffering from thyroid disease. Participants without

thyroid disease were defined as individuals who answered "no" to the above-mentioned questions.

Assessment of sleep duration

Sleep duration was assessed by the following questions: (1) On the week-day, what time did you go to sleep and wake up? (2) On the weekend, what time did you go to sleep and wake up? Using these questions, we calculated the average sleep duration on weekdays and weekends. We classified individuals into three groups according to previous research [11]: insufficient sleepers (<7 hour/day), normal sleepers (7-8 hour/day), and prolonged sleepers (≥ 9 hour/day).

Covariates

The following covariates were obtained using a standardized questionnaire in the KNHANES: sex, age, household income, education, marital status, current smoking, high-risk alcohol consumption, body mass index, working hours, physical activity, and year. The participants were stratified by age into five groups: 19-29 years, 30-39 years, 40-49 years, 50-59 years, and ≥ 60 years of age. The participants were stratified by household income into four categories: low, low-moderate, moderate-high, high. The individuals were divided by education into four groups: elementary school, middle school, high school, and college and above. Current smoking was defined as participants who smoked >100 cigarettes in their lifetime and current smokers [12]. High-risk alcohol consumption was defined as the consumption of more than 14 drinks per week for men and 10 drinks per week for women [11]. Body mass index (BMI) was stratified into three groups: underweight ($\text{BMI} < 18.5 \text{ kg/m}^2$), normal ($18.5 \text{ kg/m}^2 \leq \text{BMI} < 25 \text{ kg/m}^2$), and obese ($\text{BMI} \geq 25 \text{ kg/m}^2$) [13]. Working hours per week were classified into five groups: not working, <20, 20-39, 40-59, and ≥ 60 [14]. Physical activity was defined as moderate-intensity physical activity for more than 150 minutes per week, high level of physical activity for more than 75 minutes, or a mix of moderate-and high-intensity physical activity [15].

Statistical analysis

We assessed the association between sleep duration and the prevalence of thyroid disease according to sex. A chi-squared test was performed to assess baseline characteristics. Multiple logistic regression analyses were performed to calculate odds ratio (OR) and 95% confidence interval (CI) for general characteristic and thyroid disease. Sleep duration and thyroid

Table 1. General characteristics of study population in the Korea National Health and Nutrition Examination Surveys 2016-2018

Variables	Prevalence of thyroid disease						p-value
	Total		No		Yes		
	n	%	n	%	n	%	
Sleep duration (h)							0.630
Insufficient (<7)	5,423	30.9	5,200	95.9	223	4.1	
Normal (7-8)	8,116	46.2	7,807	96.2	309	3.8	
Prolonged (≥9)	4,016	22.9	3,863	96.2	153	3.8	
Sex							<0.000
Men	7,641	43.5	7,531	98.6	110	1.4	
Women	9,914	56.5	9,339	94.2	575	5.8	
Age (y)							<0.000
19-29	2,121	12.0	2,093	98.7	28	1.3	
30-39	2,770	15.8	2,681	96.8	89	3.2	
40-49	3,223	18.4	3,101	96.2	122	3.8	
50-59	3,339	19.0	3,150	94.3	189	5.7	
≥60	6,102	34.8	5,845	95.8	257	4.2	
Household income							0.152
Lowest	3,365	19.2	3,241	96.3	124	3.7	
Low-moderate	4,247	24.3	4,068	95.8	179	4.2	
Moderate-high	4,803	27.4	4,637	96.5	166	3.5	
Highest	5,094	29.1	4,880	95.8	214	4.2	
Missing	46						
Education							0.206
Elementary school	3,626	20.7	3,474	95.8	152	4.2	
Middle school	1,778	10.1	1,698	95.5	80	4.5	
High school	5,609	32.0	5,389	96.1	220	3.9	
≥ College	6,521	37.2	6,289	96.4	232	3.6	
Missing	21						
Marital status							<0.000
Married	14,600	83.2	13,963	95.6	637	4.4	
Unmarried	2,955	16.8	2,907	98.4	48	1.6	
Current smoking							<0.000
No	14,363	82.0	13,748	95.7	615	4.3	
Yes	3,148	18.0	3,080	97.8	68	2.2	
Missing							
High-risk alcohol consumption							0.000
No	15,490	88.4	14,857	95.9	633	4.1	
Yes	2,024	11.6	1,975	97.6	49	2.4	
Missing	41						
Body mass index							0.080
Underweight	654	3.7	638	97.6	16	2.5	
Normal	10,738	61.4	10,299	95.9	439	4.1	
Obesity	6,104	35.0	5,875	96.3	229	3.8	
Missing	59						
Working hours per week							<0.000
Not working	5,491	31.3	5,203	94.8	288	5.2	
<20	1,674	9.5	1,610	96.2	64	3.8	
20-39	2,910	16.6	2,805	96.4	105	3.6	
40-59	6,043	34.4	5,865	97.1	178	3.0	
≥60	6,928	39.5	6,590	95.1	338	4.9	
Missing	25						
Physical activity							0.691
No	9,968	56.9	9,573	96.0	395	4.0	
Yes	7,542	43.1	7,252	96.2	290	4.0	
Missing	45						
Total	17,555	100.0	16,870	96.1	685	3.9	

Table 2. The association between general characteristic and prevalence of thyroid disease among Korean adults in the Korean National Health and Nutrition Examination Surveys 2016-2018

Variables	Prevalence of thyroid disease			
	OR	95% CI		p-value
Sleep duration (h)				
Insufficient (< 7)	1.00	0.84	1.20	0.804
Normal (7-8)		Reference		
Prolonged (≥ 9)	1.05	0.86	1.29	0.605
Sex				
Men		Reference		
Women	4.52	3.56	5.73	<0.000
Age (y)				
19-29		Reference		
30-39	2.08	1.24	3.49	0.339
40-49	2.43	1.44	4.11	0.585
50-59	3.88	2.29	6.58	<0.000
≥ 60	3.30	1.91	5.70	0.001
Household income				
Lowest		Reference		
Low-moderate	1.21	0.94	1.55	0.221
Moderate-high	1.02	0.78	1.33	0.245
Highest	1.23	0.94	1.61	0.153
Education				
Elementary school		Reference		
Middle school	1.24	0.92	1.65	0.820
High school	1.40	1.07	1.82	0.153
≥ College	1.47	1.10	1.97	0.062
Marital status				
Married	1.19	0.80	1.77	0.402
Unmarried		Reference		
Current smoking				
No		Reference		
Yes	1.15	0.86	1.54	0.342
High-risk alcohol consumption				
No		Reference		
Yes	1.00	0.73	1.38	0.986
Body mass index				
Underweight	0.64	0.38	1.07	0.078
Normal		Reference		
Obesity	1.02	0.86	1.21	0.098
Working hours per week				
Not working	1.26	1.02	1.56	0.334
< 20	1.05	0.77	1.42	0.062
20-39	0.94	0.73	1.21	0.007
40-59		Reference		
≥ 60	1.19	0.85	1.66	0.281
Physical activity				
No	0.92	0.78	1.08	0.281
Yes		Reference		

OR, Odds ratio; CI, confidence interval.

Adjusted for sex, age, household income, education, marital status, current smoking, high-risk alcohol consumption, body mass index, working hours, physical activity, and sleep duration.

disease according to sex were used for multiple logistic regression analyses. Statistical significance was set at $p < 0.05$. SAS 9.4 (SAS Institute Inc., Cary, NC, USA) was used for all statistical analyses.

Ethical approval

The KNHANES VII was approved by the institutional review board of the Korea Centers for Disease Control and Prevention for the 3rd year (2018-01-03-P-A).

RESULTS

The general characteristics of the study population are summarized in Table 1. The study included 7,641 men and 9,914 women. There were 685 and 16,870 patients with and without thyroid disease, respectively. The prevalence of thyroid disease was 1.4% and 5.8% in men and women, respectively. Approximately, 4.1%, 3.8%, and 3.8% of the cases involving insufficient sleep, normal sleep, and prolonged sleep were associated with the prevalence of thyroid disease. Statistical significance was observed for sex, age, marital status, current smoking, and working hours among participants with thyroid disease (p -value < 0.0001 , respectively).

Table 2 shows that the association between general characteristic and thyroid disease among South Korean adults. Women were statistically significant for thyroid disease (OR=4.52, 95% CI=3.56-5.73). However, the prevalence of thyroid disease was not associated with sleep duration.

In the subgroup analysis, We compared sex differences in the association between sleep duration and the prevalence of thyroid disease among South Korean adults (Figure 1). Among men, insufficient sleep (OR=1.85,

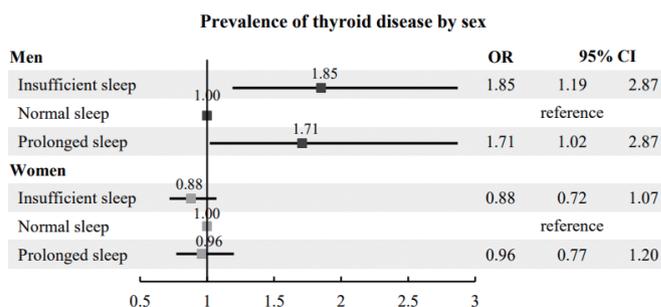


Figure 1. The sex difference in the association between sleep duration and prevalence of thyroid disease among South Korean adults. Results are demonstrated odds ratios and 95% confidence intervals. Adjusted for age, household income, education, marital status, current smoking, high-risk alcohol consumption, body mass index, working hours, physical activity, and sleep duration.

95% CI=1.19-2.87) and prolonged sleep (OR=1.71, 95% CI=1.02-2.87) were associated with the prevalence of thyroid disease; however, the same was not observed for women.

DISCUSSION

The results of the present study demonstrated that sleep duration was not associated with the prevalence of thyroid disease. However, we found that there was a sex difference between sleep duration and the prevalence of thyroid disease. In subgroup analysis, insufficient and prolonged sleep was related to the risk of thyroid disease for men. However, no statistically significant association was observed in women.

Most previous studies have confirmed the effects of sleep on various diseases and mortality, including cardiometabolic health [1], depression [16], chronic pain [3], increased risk of death [17], myriad adverse behavioral consequences [2] and metabolic syndrome [5]. Based on those studies, our study defined 7-8 hours as adequate sleep duration which was found to be preventive factor for thyroid disease. However, few studies have investigated the influence of sleep on thyroid function by sex, and there is a lack of information concerning the topic.

In previous studies, subclinical thyroid disease was associated with short and long sleep durations [8]. Based on this study, short sleep was increased in hyperthyroidism; however, the same was not observed in hypothyroidism. Further, short sleep was associated with a high probability of TSH suppression. Long sleep duration was associated with increased TSH secretion and subclinical hypothyroidism. In addition, both short sleep and long sleep are increased in hyperthyroidism [8].

Although there are few studies detailing sleep duration and thyroid disease, several studies have shown that changes in serum concentrations of thyroid stimulating hormone (TSH), free triiodothyronine (fT3), and free thyroxine (fT4) were controlled by circadian rhythm and partial sleep and they impacted secretory activity and thyroid function [9,18-20]. Several studies have evaluated the influence of sleep on TSH, fT3, and fT4, which are affected by thyroid and other diseases [9]. In previous studies, women were higher 24 h-fT4 concentrations than men. In both men and women, partial sleep loss was related to a decline in free T4 and TSH; however, the results indicated that women had a statistically significant association [20]. Ferdinand [19] showed that elderly men had lower average nocturnal TSH levels compared to young individuals. In these sleep loss studies, sleep restriction for two consecutive nights among

young men influenced the thyrotrophic axis [9]. Serum concentrations of fT3 and fT4 were increased, and serum TSH levels were slightly elevated in the evening hours [9]. Additionally, studies of thyrotropin secretion profiles demonstrated that TSH concentrations were slightly higher in men than in women at night [18].

According to our results, sleep duration was not associated with the prevalence of thyroid disease compared to a previous study [8]. A previous study explained that sleep duration exerted an influence on subclinical hyperthyroidism and subclinical hypothyroidism with thyroid hormone [8]. Further, our study indicated a statistical significance for men, when the correlation between insufficient sleep and prevalence of thyroid disease was analyzed by sex. Our study data from KNHANES 2016-2018 were not investigated for serum concentrations of TSH, fT3, and fT4. We could not confirm the mechanism underlying the association between sleep duration and the prevalence of thyroid disease. Therefore, our study is based on several previous studies. Thus, more studies are required to examine the influence of sleep duration on thyroid disease by sex, sleep quality, large population, and nationally representative data.

This study had several strengths. First, this study used a nationally representative sample with a large population compared to previous studies. To our knowledge, this is the first study detailing sex difference between sleep duration and the prevalence of thyroid disease. Second, various covariables were used in our studies and defined as thyroid disease with physician diagnosis and current prevalence to ensure precise measurement. Third, we investigated the wakeup time and bedtime on weekdays and weekends, respectively, using KNHANES questionnaires. Using these individuals' sleep time, we calculated the average sleep duration on weekdays and weekends.

However, there are some limitations to our study. First, sleep quality was not analyzed in the present study. The sleep quality and sleep duration affected thyroid disease [21-24], so it should be included in future studies. Second, there was no information about TSH, fT4, and fT3 in the KNHANES from 2016 to 2018. Therefore, thyroid hormones could not be measured. However, we could provide exact measurements as we used the KNHANES questionnaires for information concerning physician diagnosis and the prevalence of thyroid disease. Third, hyperthyroidism, hypothyroidism, thyroid positive nodules and Hashimoto thyroiditis were included thyroid disease in KNHANES. This study was not investigated in detail, such as the relationship between hyperthyroidism and sleep duration.

CONCLUSIONS

In conclusion, sex differences showed a relationship between sleep duration and thyroid disease. We propose to add thyroid hormones in general health examination blood tests and include thyroid cancer in the national cancer examination for examination once every two years for men and women. Additional studies are needed to confirm the association of sleep duration and thyroid disease with sleep quality according to sex and analyses with other interesting variables.

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국문초록

한국성인의 수면시간과 갑상샘 질환 사이의 관계성에 대한 성별차이

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목적: 본 연구는 한국 성인의 수면시간과 갑상샘 유병률의 관계성에 대해 성별 차이를 파악하고자 한다.

방법: 본 단면연구는 2016년부터 2018년까지 국민건강영양조사에 참여한 성인 17,555명이 포함되었다. 수면시간은 3가지로 분류하였다 (불충분한 수면, 7시간 미만; 정상 수면, 7-8시간; 장시간 수면, 9시간 이상). 일반적 특성을 측정하기 위해 카이제곱 검정을 실시하였다. 일반적 특성과 갑상샘 질환 유병률 간의 관계를 확인하기 위해 다중 로지스틱 회귀분석을 사용하였다. 하위그룹 분석에서, 다중 로지스틱 회귀분석은 성별에 따라 수면시간과 갑상샘 질환 유병률 간의 관계성을 알기 위해 시행되었다.

결과: 불충분한 수면과 장시간의 수면을 취한 남성은 정상 수면과 비교하였을 때 갑상샘 질환의 위험성이 증가하였다(불충분한 수면: OR=1.85, 95% CI=1.19-2.87; 장시간 수면: OR=1.71, 95% CI=1.02-2.87).

결론: 본 연구는 불충분하고 장시간의 수면을 취한 남성은 갑상샘 질환과 관련성이 있다. 추후 연구에서는 성별에 따른 수면시간과 갑상샘 질환의 관계성을 수면의 질과 함께 고려할 필요가 있다.

주제어: 성별 차이, 수면시간, 갑상샘 질환